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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,641	09/15/2003	David Standring	06171.105097 (IDX 1021 US	2664

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EXAMINER	
MCINTOSH III, TRAVISS C	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 12/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	10/662,641	STANDRING ET AL.	
	Examiner	Art Unit	
	Traviss C. McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *26-73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25,74 and 75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/4/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(e) to the provisional application 60/410,675 filed September 13, 2002.

Election/Restrictions

Applicant's election of Group I in the reply filed on September 15, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

As such, claims 26-73 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Additionally, the portion of claims 1-5 drawn to using compounds where X is SO_2 or CH_2 is also being withdrawn as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-25 and 74-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-25 and 74-75 are drawn to methods of treating a host infected with a drug-resistant form of HBV by administering various β-L-2'-deoxynucleosides, but the claims do not state to whom the nucleosides are intended to be administered to. Including in the claim who the composition is to be administered to would obviate the instant rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

Determining the scope and contents of the prior art.
Ascertaining the differences between the prior art and the claims at issue.
Resolving the level of ordinary skill in the pertinent art.
Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-25 and 74-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gosselin et al. (US Patent 6,395,716 B1) in view of Wu (US Patent 6,855,346 B2).

Claim 1 of the instant application is drawn to a method of treating a host infected with a drug-resistant form of HBV by administering an effective amount of a β-L-2'-deoxynucleoside, or a salt, ester, or prodrug thereof. Claims 2 and 3 provide the deoxynucleoside is a deoxythymidine or deoxycytidine. Claim 4 provides that the HBV exhibits a mutation at the 552

codon from methionine to valine in the DNA polymerase region. Claims 5-25 provide various nucleoside structures for the β-L-2'-deoxynucleoside. Claims 74 and 75 provide that the host is a mammal, and that the mammal is a human.

Gosselin et al. disclose methods of treating HBV by administering various β-L-2'-deoxynucleosides or salts thereof (see purine and pyrimidine nucleosides in columns 3-5). Gosselin et al. teach that drug resistant variants of HBV can emerge after prolonged treatment with an antiviral agent. Gosselin et al. teach that drug resistance most typically occurs by mutation of a gene that encodes an for an enzyme that is used in the viral life cycle, most typically the case in HBV being the DNA polymerase (see column 12, lines 23-28). What is not taught is to administer to drug-resistant forms which exhibit a mutation at the 552 codon from methionine to valine.

Wu teaches that lamivudine-resistant viruses have a characteristic amino acid substitution over tyrosine-methionine-aspartate-aspartate (YMDD) motif on the RNA-dependent DNA polymerase (column 4, lines 45-49). Wu teaches that the methionine at codon 552 is either replaced by an isoleucine or valine (M552V).

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer the β-L-2'-deoxynucleosides of Gosselin et al. in patients with all types of drug-resistant mutations, including the M552V mutations, as Wu teaches that this is a common mutation in drug-resistant HBV. Gosselin et al. disclose β-L-2'-deoxynucleosides which overlap in structure with the compounds claimed in the instant application. It is noted that the compounds of claims 14, 15, 16, 23, 24, and 25 are seen to be obvious variants to the compounds of claims

13 and 22 respectively, as claims 14-16 and 23-25 are prodrugs of claims 13 and 22. Gosselin et al. state that the compounds used can be prodrugs, such as an acyl containing group (column 3, lines 46-62). It is well established in the art that the ester forms of claims 14-16 and 23-25 are hydrolyzed *in vivo* in to the active metabolites of claims 13 and 22 respectively. Both Gosselin et al. and Wu discuss problems with drug-resistant HBV and Gosselin et al. states that it has been demonstrated that the efficacy of a drug against HBV can be prolonged, augmented, or restored by administering the compound in combination or alternation with a second, or even a third antiviral compound that induces a different mutation from that caused by the principle drug (see column 12, lines 28-32). Moreover, Gosselin et al. teach that the anti-HBV activity of their β-L-2'-deoxynucleosides (including thymidines, uridines, cytidines, adenosines, guanosines, and inosines), prodrugs, phosphates, or salts thereof can be enhanced by administering two or more of in combination or alternation. Wu teaches that administering the art recognized anti-HBV agent lamivudine causes mutations which are frequently located at the 552 codon, wherein the mutated HBV become drug resistant. Gosselin et al. teach to administer their β-L-2'-deoxynucleosides in combination with other drugs, including 3TC (which is known to be lamivudine, see column 12, line 47 and column 37, line 21). One would be motivated to administer β-L-2'-deoxynucleosides to the claimed drug-resistant HBV because Wu teaches that the lamivudine administered HBV would mutate at the 552 codon as claimed, and Gosselin teaches to administer β-L-2'-deoxynucleosides in combination or alternation with lamivudine to treat the mutated and thus lamivudine-resistant HBV (M552V). It would be obvious of one of ordinary skill in the art at the time of the invention to administer the β-L-2'-deoxynucleosides to any drug-resistant HBV with these references before them. The M552V mutations are known to

occur in lamivudine administered HBV and β-L-2'-deoxynucleosides are known to be effective in combination therapy with lamivudine.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C. McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh III

December 9, 2005

Shaojia A. Jiang
Supervisory Patent Examiner
Art Unit 1623

SAJ 12/9/05